Stimulation of glomerular and tubular cell growth by antioxidant enzymes and their inhibitors

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Kidney glomerular or tubular cells from adult guinea pigs were grown in primary culture in a chemically defined media containing only Waymouth's media MB752/1, insulin, transferrin, triiodothyronine, selenium, and fibronectin. To test the effect of the antioxidant enzymes superoxide dismutase (SOD) or catalase and their inhibitors on cell growth, equal numbers of glomeruli or tubular cells were plated in Costar wells and chemically defined media was added containing either: a) no additional additives, b) SOD, c) catalase, d) diethyldithiocarbamate (DDC), an inhibitor of SOD, or 3) 3-amino-1,2,4-triazole, an inhibitor of catalase. Each day after inoculation the number of cells per well was counted using phase microscopy. Paradoxically, either antioxidant enzymes or their inhibitors stimulated both glomerular and tubular cell growth; SOD stimulation was unique in that it required selenium. Many other enzymes and low molecular weight compounds tested did not stimulate growth of either cell type. We have hypothesized from these results that cell growth stimulation is dependent in cell surface oxygen concentration since experiments in other laboratories have suggested that SOD is not able to penetrate intact cells. Experiments are currently in progress to test this hypothesis.

OXIDATIVE STRESS IN INTACT CELLS AND ORGANS: REDOX CYCLING AND THE FORMATION OF SINGLET OXYGEN, MIXED DISULFIDES AND GLUTATHIONE DISULFIDE.

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Drugs and other chemicals may elicit socalled oxidative stress associated with the formation of aggresive oxygen species. Low-level chemiluminescence affords -- with some proviso -- a readout of singlet molecular oxygen levels in cells, and recent work on menadione, paraquat and t-butyl hydroperoxide will be presented.

Mixed disulfides of glutathione with membrane proteins and enzymes and with coenzyme A as well as glutathione disulfide are formed at increased rates during oxidative stress. This has repercussions on several metabolic processes and is of potential regulatory importance. Biliary GSSG efflux from perfused liver provides useful non-invasive information.